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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,388	05/25/2007	Natacha Depaola	3230.3009 US	2542

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,388	DEPAOLA ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-28 are pending in the present application, and they are subjected to the following restrictions.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 5-6, 12, 16-17, drawn to a method of establishing or restoring gap junctional intercellular communication (GJIC) in an endothelial cell layer in vitro by exposing an endothelial cell layer to hemodynamic forces; an endothelial cell monolayer produced by the same method and a vascular implant comprising the same endothelial cell layer.

Group II, claims 7-8, 13, 18, drawn to a method of establishing or restoring gap junctional intercellular communication (GJIC) in an endothelial cell layer in vitro by inducing expression of at least one vascular gap junction protein or combination of vascular gap junction proteins in an endothelial cell layer comprising recombinant endothelial cells; an endothelial cell monolayer produced by the same method and a vascular implant comprising the same endothelial cell layer..

Group III, claims 9-11, 14 and 19, drawn to a method of establishing or restoring gap junctional intercellular communication (GJIC) in an endothelial cell layer in vitro by exposing an endothelial cell layer comprising recombinant endothelial cells capable of expressing at least one vascular gap junction protein or combination of vascular gap junction proteins to hemodynamic forces; an endothelial cell monolayer produced by the same method and a vascular implant comprising the same endothelial cell layer.

Group IV, claims 15 and 23-28, drawn to a vascular implant comprising a matrix with a monolayer of recombinant endothelial cells capable of expressing at least one vascular gap junction protein or combination of vascular gap junction proteins and a method for manufacturing the same implant.

Group V, claims 20-21, drawn to a method for treating a patient in need of a vascular implant comprising a matrix with a monolayer of recombinant endothelial cells capable of expressing at least one vascular gap junction protein or combination of vascular gap junction proteins and the endothelial cell layer is exposed to hemodynamic forces.

Group VI, claim 22, drawn to a method for treating a patient in need of a vascular implant comprising an implant matrix being seeded with cDNA encoding Cx37, Cx40, Cx43 or a combination thereof.

Claims 1-4 link a plurality of different inventions of Groups I-V. This is because a method of establishing or restoring GJIC in an endothelial cell layer in vitro by modulating the expression, organization and assembly of at least one vascular gap junction protein or a combination of gap junction proteins encompass biophysical manipulation (Group I), genetic manipulation (Group II) and a combination of both biophysical manipulation and genetic manipulation (Group III).

Upon the allowance of the linking claims, the restriction requirement as to the linked invention shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims or the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable.

See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-132(CCPA 1971). See also MPEP 804.01.

The technical feature linking Groups I-VI appears to be that they all relate to an endothelial cell layer that has been exposed to hemodynamic forces, genetic manipulation for expressing at least one vascular gap junction protein or a combination of both hemodynamic forces and genetic manipulation.

At the effective filing date of the present application (10/03/2003), at least Flugelman et al (Circulation Research 70:348-354, 1992) already subjected a monolayer of endothelial cells adhered to stent surfaces to pulsatile flow for 2 hours (see at least the abstract and Figure 2); DePaola et al (PNAS 96:3154-3159, 1999; IDS) investigated spatial and temporal regulation of gap junction connexin43 in vascular endothelial cells exposed to controlled disturbed flows in vitro (see at least the abstract); and Seul et al (US 2003/0215424) transfected endothelial cells in vitro with a recombinant vector encoding a member of a connexin family of polypepitdes (see at least Summary of the Invention and examples 3 and 5).

Therefore, the technical feature linking the inventions of Groups I-VI does not constitute a special technical feature a defined by PCT Rule 13.2, as it does not differentiate the claimed subject matter a whole over the prior art. Since according to Rule 13.2 PCT the presence of such a common or corresponding special technical feature is an absolute prerequisite for unity to be established, and given that there does not appear to be any other technical feature common to the claimed subject matter as a

whole which might be able to fulfill this role, the currently claimed subject matter lacks unity of invention according to Rule 13.1 PCT.

Consequently, the claimed subject matter is restricted into the above Groups of Inventions for the following reasons.

The compositions in Group I-IV are different one from the others as well as the methods for making the same corresponding compositions with different method steps and starting materials. For example, the endothelial cells in Group I are not recombinant cells; the recombinant endothelial cells of Group II are not subjected to hemodynamic forces whereas the recombinant endothelial cells of Group III are required to expose to hemodynamic forces; and in contrast to both compositions of Groups II and III the vascular implant of Group IV contains a matrix derived from various sources in addition to a monolayer of recombinant endothelial cells.

The methods of Groups I-VI are different methods with different method steps and starting materials as well as different desired end-results. Unlike the methods of Groups I-IV directing to methods for preparing different endothelial cell monolayers in different conditions as already mentioned in the preceding paragraph, the methods in Groups V-VI are directed to therapy methods. The therapy method of Group V is different from the therapy method of Group VI in using a vascular implant containing a matrix and a monolayer of recombinant endothelial cells that have been exposed to hemodynamic forces; whereas the therapy method of Group VI simply requires the use of an implant matrix with cDNA coding for Cx37, Cx40, Cx43 or combinations thereof.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the topical delivery system of Group I can be used for treatment of a metabolic disease of Group III.

Inventions IV and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the composition of Group IV can be used in a screening method to identify compounds that modulate GJIC process. It is further noted that the method of Group V does not require the compositions in Groups I-III.

The method of Group VI does not require any composition in Groups I-IV.

Because the currently claimed subject matter lacks unity according to Rule 13.1 PCT for the reasons set forth above, restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance

with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17 (h).

Species restriction:

Should Applicants elect anyone of Group I-VI, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

(a) Cx37; (b) Cx40; (c) Cx43 and (d) a single specific combination of (a)-(c).

Additionally, should Applicants elect Group IV, this application contains claims directed to more than one species of the generic invention. These species are

deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of an implant matrix are as follows:

(a) acellular or decellularized tissues; (b) non-biodegradable, natural or synthetic polymers; and (c) resorbable materials.

(I) **Furthermore, should Applicants elect the above species (a)**, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of an implant matrix are as follows:

A single specifically named matrix recited in the Markush group of claim 28.

(II) **Furthermore, should Applicants elect the above species (b)**, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of an implant matrix are as follows:

A single specifically named matrix recited in the Markush group of claim 26.

(III) **Furthermore, should Applicants elect the above species (c)**, this application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species of an implant matrix are as follows:

A single specifically named matrix recited in the Markush group of claim 27.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

Each of the aforementioned species is different structurally and has different properties one from the others. Therefore, each different structure can be considered to be a "special technical feature"; and therefore the listed species lack the same or corresponding special technical features.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN/
Primary Examiner, Art Unit 1633